UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

January 5, 2000

MEMORANDUM

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

SUBJECT: **Oxamyl** PC Code 103801. Decision from the HED Metabolism Assessment Ad Hoc Review Committee Meeting on Oct 27, 1999. Case 0253. DP Barcode D260911.

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THROUGH: Richard A. Loranger, PhD,
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TO: George Kramer, PhD,
Secretary of MARC
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QUESTIONS TO METABOLISM ASSESSMENT REVIEW COMMITTEE

1. Is the tolerance expression for oxamyl (**40 CFR §180.303**) which presently includes oxamyl and oxime appropriate?

2. Are any metabolites of oxamyl in addition to oxime to be included in any risk assessment?

Conclusions:

1. The Committee concluded that the main metabolite of oxamyl, (oxime) is not likely to be a potent acetyl cholinesterase inhibitor and therefore need not be included in the risk assessment from a toxicological perspective. However, it is not possible to exclude it from the tolerance expression since the analytical methods used for the field trials which established the tolerance, convert oxamyl to oxime by employing a hydrolysis step. The concentrations of oxamyl reported by these methods will include an unknown amount of

oxime; consequently, both oxamyl and oxime metabolite will be included in the tolerance expression. This is consistent with Codex. The Committee noted that although other toxicological effects were observed from administration of oxamyl, regulating based on the cholinesterase endpoint would be protective of these effects.

2. There was a concern raised about the levels of radioactive thiocyanate found in an exaggerated rate (25x) radioactive ruminant feeding study (up to 2.0 ppm in milk). Subsequently, a brief literature search was done to find estimates of thiocyanate in normal human serum and foods.

In a large Norwegian health study (1) the mean serum thiocyanate levels were 33.9 umol/l for the control population (non-smoking males) corresponding to ~2.3 ppm. In a small thiocyanate ingestion study from India (2) non-smoking controls showed thiocyanate levels of 90.8 umol/l corresponding to 6.5 ppm.

In a Swedish clinical study (3), levels of blood serum thiocyanate were studied in volunteers administered milk fortified with sodium thiocyanate (20 ppm, 200 ml/dose, twice daily for 3 months). Mean serum thiocyanate concentrations in 32 subjects at time 0 were 4.0 mg/l (4 ppm). At 3 months, at apparent steady state, the mean serum thiocyanate concentration was 7.0 mg/l (7 ppm).

In a dietary thiocyanate study (4) thiocyanate levels were measured in Brassica (cauliflower, Brussels sprouts, cabbage, red cabbage) and ranged from 3.6-48.5 mg/ 200 g vegetable. These values correspond to thiocyanate concentration ranging from ~20 ppm to ~250 ppm.

In a German study (5), thiocyanate levels were measured in milk obtained from 7 healthy lactating cows; mean levels of thiocyanate ranged from 1.7 to 2.0 ppm. In a Swedish study (3) it was noted by the authors that the concentration of thiocyanate in cow milk ranges from 3 to 5 mg/l (3-5 ppm).

The thiocyanate content in a variety of foodstuffs was measured in milk, cheese, meat, salad (parsley, celery, leek, cucumber), and cabbage (1). Thiocyanate was not detected in bread, potato, apple, orange, carrot, onion, or fish. The data were expressed in a rather unusual form (umol/l per kg). If we assume that the measured concentration resulted from using the 1kg sample then the data can be expressed as umol/l. That is in 1 l of milk, for example, there were measured 40 -50 umol thiocyanate. Converting to mg and subsequently ppm, the range for cabbage was determined to range from 21 ppm to 355 ppm. These values are similar to those found in reference 3.

Given that relatively high concentrations of thiocyanate exist in normal individuals and foodstuffs it is unlikely that the thiocyanate metabolite formed as a consequence of exposure to oxamyl will contribute a substantial amount to the background exposure to thiocyanate through normal human metabolic processes and consumption of foods containing naturally occurring amounts of thiocyanate.

3. With respect to drinking water, the parent is not found often, but can be observed in areas with acidic pH. Although more recent monitoring data separate parent and oxime, EFED could not provide a concentration for the oxime at this time. Modeling data based on oxamyl alone would be acceptable for risk assessment considering the relative lack of toxicological concern over the oxime. Monitoring data which reflect total residues converted to oxime could also be used for risk assessment with respect to drinking water.

References

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3. Dahlberg P.-A., Bergmark, A., Bjorck, L., et al. Intake of Thiocyanate by Way of Milk and its Possible Effect on Thyroid Function. Am. J. Clin. Nutr. 1984; 39:416-420.

4. Olea F, Parras P. Determination of Serum Levels of Dietary Thiocyanate. Journal of Analytical Toxicology 1992; 16: 258-260.

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Meeting Attendees: MARC- Alberto Protzel, Richard Loranger
HED Scientists- John Punzi, Christina Jarvis, Diana Locke, Guruva Reddy
EFED Scientists- E. Laurence Libelo, Nick Federoff

cc: JSPunzi(RRB2). Oxamyl Reg. Std. File, Oxamyl SF, RF.
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